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ORIGINAL ARTICLE

Comparison of the efficacy of dexketoprofen and diclofenac in treatment of non-specific low back pain

Krzysztof Brzeziński[1], Jerzy Wordliczek[2]

[1] *Outpatient Pain Clinic, Institute of Rural Health, Lublin, Poland*
[2] *Department of Pain Treatment and Palliative Care, Jagiellonian University, Collegium Medicum, Cracow, Poland*

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Abstract

Work-related loads, improper lifestyle, increasing obesity, and lack of adequate prophylaxy render low back pain (LBP) one of the most common causes of chronic pain worldwide.

Objective. The aim of the study was to compare the effect of two analgesic drugs on the effectiveness of therapy measured by pain intensity. and the degree of disability during treatment of chronic low back pain syndrome

Material and method. The retrospective analysis involved 185 patients undergoing treatment for chronic low back pain syndrome with dexketoprofen (DEX) and diclofenac (DIC). Patients' gender. place of residence. cause of the pain as well as pain intensity in the visual-analogue scale (VAS) and the disability degree (Oswestry Disability Index – ODI) were analysed.

Results. From the first week of treatment to the end of the observation. the DEX group exhibited significantly lower values of pain intensity on the disability index. The correlation coefficients between the parameters were significantly higher in the DEX group. Analysis of variance demonstrated that the choice of NSAIDs was the most significant factor determining the effectiveness of the treatment.

Discussion. The cause of the pain and place of residence did not have any impact on the treatment efficacy. The pharmacological properties of dexketoprofen contribute to its beneficial effect on the therapy used. which validates the potential use of DEX in LBP management.

Summary. The significantly increased correlation between the aforementioned parameters suggests that administration of dexketoprofen in the management of non-specific low back pain results in a more rapid return to full physical activity and therefore more prompt return to work.

Keywords

low back pain, dexketoprofen, diclofenac, pain treatment, Oswesrty Disability Index

INTRODUCTION

Disorders of the lumbar spine (LBP) are prevalent in all western societies [1, 2, 3, 4, 5]. It is extremely disturbing that there are increasing numbers of adolescent people with such severe symptoms that force doctors to recommend hospitalization [6, 7].

Investigations conducted by Kuslich [8] demonstrated that the sites responsible for the appearance of pain symptoms may equally be the intervertebral discs. facet joints. ligaments. fascia. nerve roots and dura structures. When these structures are pathological. the syndrome is classified as Nonspecific Low Back Pain. in contrast to pain caused by nerve root compression called Sciatica.

Work-related loads [9]. improper lifestyle [10]. increasing obesity. and lack of adequate prophylaxis contribute to the high position of LBP on the list of causes of chronic pain worldwide [11] which still remains one of the principal causes of public health problems [12].

Non-steroidal anti-inflammatory drugs (NSAID) are the most commonly applied medications in LBP management. They differ in their chemical composition. anti-inflammatory and analgesic potency [13]. and activity against particular types of cyclooxygenase [14, 15, 16, 17]. Medical doctors usually choose drugs solely on the basis of their knowledge of the drug efficacy [18]; therefore. an objective comparative research into the use of particular drugs for specific indications is valuable [19, 20, 21].

Diclofenac is an aminophenylacetic acid derivative with a potent anti-inflammatory. analgesic. and antipyretic activity through inhibition of cyclooxygenases. with a considerably greater affinity to their constitutive (COX-1) rather induced (COX-2) form. Another NSAID is dexketoprofen (propionic acid derivative). an S-isomer isolated from a racemic ketoprofen mixture. The study carried out by Carabaza [22] and Cabre [23] demonstrated that the dextrorotatory stereoisomer is a several-fold stronger inhibitor of cyclo-oxygenase than the non-isolated racemic mixture.

Objective. The aim of the study was to compare the effect of two analgesic drugs on therapy efficacy measured by pain intensity and the degree of disability during treatment of chronic low back pain syndromes. The drugs tested belong to different pharmacological groups characterized by a similar profile and comparable duration of action.

Address for correspondence: Krzysztof Brzeźiński, Institute of Rural Health, Jaczewskiego 2, 20-090 Lublin, Poland
e-mail: k.brzezinski@op.pl

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MATERIALS AND METHOD

The retrospective analysis involved medical records from 185 patients of the Outpatient Pain Clinic. Institute of Rural Health in Lublin. south-east Poland. treated for chronic pain of the lumbosacral spine.

The investigations were carried out in adult patients who had previously been treated for non-specific low back pain for over two years. and had had six appointments at the clinic on a weekly basis. Past operative treatment of the lumbar spine or for cancer. and lack of compliance with the weekly visit schedule were the criteria for patient exclusion from the study.

Patients receiving dexketoprofen treatment were classified into group DEX. and those treated with diclofenac constituted group DIC.

Patients' gender. place of residence. and the cause of the pain were analysed. During successive visits scheduled at one-week intervals for six weeks. pain intensity was assessed in the visual-analogue scale (VAS) and the degree of disability estimated using the Oswestry Disability Index (ODI).

Statistical analysis. The differences between the study groups were evaluated using a univariate or multivariate analysis of variance. taking into account the degrees of freedom (Df). the value of Fisher's test. and statistical significance (p). Demographic data (place of residence. gender. and causes of pain) were analysed using the non-parametric χ^2 test with the χ^2 value. degrees of freedom (Df). and statistical significance (p).

The effect of all the analysed factors (place of residence. choice of therapy. choice of NSAID. and duration of therapy) on treatment efficacy was assessed by means of a multivariate analysis of variance. The correlations between pain intensity and degree of disability were analysed using Pearson's coefficient; the equation for the correlation curve is presented in the Figures. A p value lower than 0.05 was considered statistically significant. Statistic package Statgraphics Plus 5.1 was used in the analysis.

RESULTS

Among the 185 patients qualified for the analysis. 32 did not complete the observation schedule. In all cases of treatment intolerance. the drug was replaced by another non-steroidal anti-inflammatory drug. Tramadol or low doses of strong opioids were administered in the case of inefficacy of the treatment, and the data from these patients were subject to further analysis (Tab.1).

Table 1. Number of patients in respective groups and patients who did not complete the test schedule

Groups	No. of qualified patients	Causes of exclusion from the treatment			No. of patients who completed the test schedule
		Classified for surgical treatment	Nausea and vomit	Treatment inefficacy	
DEX	90	4	5	4	77
	48.65%	4.44%	5.56%	4.44%	85.56%
DIC	95	5	9	5	76
	51.35%	5.26%	9.47%	5.26%	80.00%
Total	185 100%	9 4.86%	14 7.57%	9 4.86%	154 83.24%

Abbreviations: DEX – dexketoprofen. DIC – diclofenac

The mean age was 61.36 lat (SD = 13.34; range 25–92). Statistical analysis performed with the use of nonparametric tests showed that the cause of pain or gender did not have a significant impact on the choice of therapy (Tab. 2). Due to the large disproportions between the groups. the place of residence was not taken into account in further analyses.

Table 2. Demographic data of patient groups

	DEX n=77 (%)	DIC n=76 (%)	Statistical significance
Females	60 (77.92%)	52 (69.33%)	χ^2=2.11; Df=3; p = 0.5489
Males	17 (22.08%)	23 (30.67%)	
Urban	56 (72.73%)	63 (82.89%)	χ^2=0.83; Df=3; p = 0.0425
Rural	21 (27.27%)	12 (15.79%)	
Discopathy	22 (28.57%)	11 (14.47%)	χ^2 = 0.83; Df=3; p=0.425
Degenerative changes	55 ()71.43%	64 (84.215%)	

DEX – dexketoprofen; DIC – diclofenac; Df – degrees of freedom

The mean values of pain intensity for the respective groups during all the examination stages are presented in Table 3 and Figure 1.

At the first encounter with the patients (stage 0) VAS pain intensity scores did not differ between the basic groups (Df=1; $F = 1.66$; p = 0.2009) and reached 6.78 cm (SD = 0.9) for DEX and 6.55 cm (SD = 1.03) for DIC.

Table 3. Numerical values of VAS pain intensity and ODI degree of disability presented as means and standard deviations in the subsequent test stages

	Stages of analyses						
	0	I	II	III	IV	V	VI
Groups				**VAS**			
DIC	6.78	4.90	3.10	2.90	2.70	2.55	2.61
SD	*0.90*	*1.01*	*1.01*	*1.01*	*1.01*	*1.07*	*1.08*
DEX	6.55	3.98	2.58	2.20	1.97	1.79	1.78
SD	*1.03*	*0.96*	*0.88*	*0.84*	*0.82*	*0.89*	*0.89*
Groups				**ODI**			
DIC	64.05	53.81	48.39	42.04	35.02	28.63	22.95
SD	*10.47*	*9.90*	*10.93*	*11.25*	*11.32*	*12.26*	*12.21*
DEX	65.32	48.32	39.39	30.71	24.79	19.54	15.68
SD	*10.56*	*9.67*	*10.60*	*9.94*	*9.70*	*10.44*	*11.51*

DIC – diclofenac; DEX – dexketoprofen; SD – standard deviation

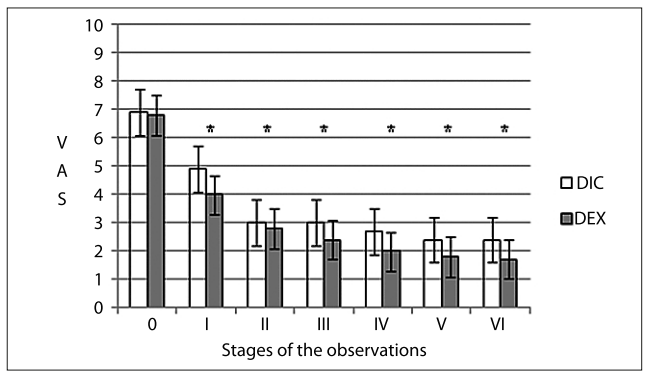

Figure 1. VAS pain intensity. Comparison of mean values in groups of patients treated with dexketoprofen (DEX) and diclofenac (DIC) during the consecutive stages of the observations
* p<0.05

After the first week of treatment (Stage 1), the pain intensity value decreased in all the patients, reaching 3.98 (SD = 0.95) for DEX and 4.90 for DIC (SD = 1.01). Significant differences between the test groups (Df=1; $F = 24.06$; p = 0.0001), which persisted throughout the observation, were demonstrated by a univariate analysis of variance, as in the case of the disability index (ODI) values. The values did not differ between the patient groups in the initial stage of the observation (Df=1; F = 45.44; p=0.5264) and decreased significantly from the first treatment stage reaching 53.81 (DS. = 9.90), for the DIC group and 48.32 (SD = 9.67) for the DEX group. In this stage, statistical significance of the differences between the described values was found (Df = 1; F = 8.72; p = 0.004). which persisted until the end of the observation. The numerical data concerning the degree of disability are presented in Table 3; Figure 2 presents the graphic illustration.

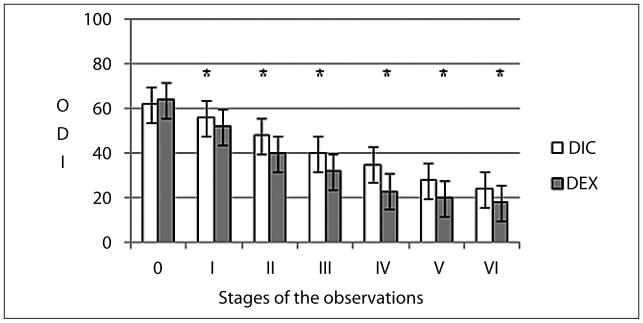

Figure 2. Degree of disability measured by Oswestry Disability Index (ODI). Comparison of mean values in patient groups treated with dexketoprofen (DEX) and diclofenac (DIC) during successive stages of observation
* – p<0.001

Analysis of the correlation between pain intensity (VAS) and degree of disability was performed and demonstrated a higher correlation between these two parameters in the group of patients receiving dexketoprofen (Fig. 3 and 4). The multivariate analysis of variance demonstrated that the choice of the NSAID had the most significant impact on treatment efficacy (Tab. 4)

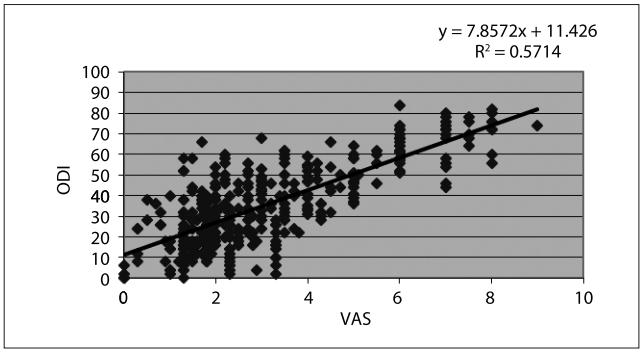

Figure 3. Graph of the curve of correlation between degree of disability measured by Oswestry Disability Index (ODI) and pain intensity in the VAS in all patients treated with dexketoprofen DEX. Correlation coefficient 0.755. The equation for the curve is given in the upper right corner

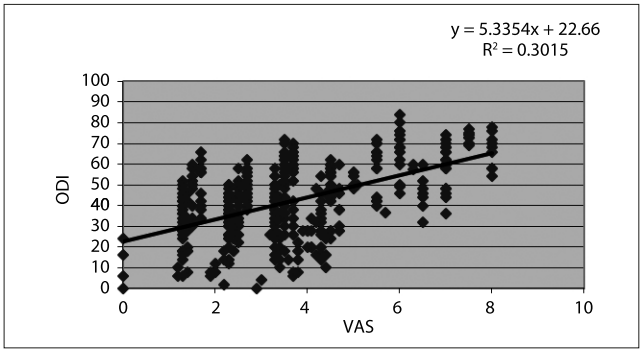

Figure 4. Graph of the curve of correlation between degree of disability measured by Oswestry Disability Index (ODI) and pain intensity in the VAS in all patients treated with diclofenac DIC. Correlation coefficient 0.549. The equation for the curve is given in the upper right corner.

Table 4. Impact of various factors on therapy efficacy. Multivariate analysis of variance

Tested factor	Degrees of freedom	Value of Fisher's test	Statistical significance
Choice of NSAID	Df=1	F=18.73	p<0.0000
Cause of pain	Df=1	F=0.06	p=0.8011
Place of residence	Df=1	F= 1.50	p=0.2227
Gender	Df=1	F= 0.05	p=0.8323

DISCUSSION

Attempts to develop the most effective therapy for non-specific low back pain are continuously being undertaken. Treatment should prevent occurrence of chronic pain [24]. and allow a prompt return to work. Appropriate pain control and restoration of physical activity are regarded by the authors as key factors for guidelines based on a meta-analysis of research papers [25, 26].

Lumbar pain constitutes a serious medical problem due to its high prevalence and disabilities accompanying this disease, which is reflected in the general condition of public health [27]. The study conducted by Fredheim et al. [28] showed a significantly poorer quality of life in patients whose disability was not associated with cancer disease. The condition analysed in the presented study should also be considered from the socio-economic aspect, since the costs of treatment are extremely high. Research carried out in the Swedish population also demonstrated that the direct costs are very high (3,100 euros per year), but the indirect costs are substantially greater and reach as much as 17,600 euros [29]. Therefore, it is crucial that the treatment methods employed ensure the regaining of full physical activity and prompt return to work.

A majority of the patients presented in the paper exhibited a substantial degree of disability confirmed by the ODI. The study has shown that application of dexketoprofen resulted in significantly more rapid reduction in both pain intensity and the degree of disability. Since the study was not randomized, the results obtained allow only a reasonable assumption that the tested drug will facilitate faster and complete recovery.

In terms of pathophysiology, in both groups, pain was classified as receptor pain, i.e. pain that can be effectively treated according to the 'WHO analgesic ladder' scheme [30, 31, 32].

In the available literature, low back pain is classified into specific pain (related to pressure exerted of pathological structures on the nerve root) and non-specific (connected with pathology of the motion segment) [25, 26, 33, 34, 35]. No classification has been reported that would differentiate the non-specific low back pain depending on the immediate cause of pain. Therefore, the material described here is in accordance with literature data, as no distinct differences were found between the decrease in pain intensity in the case of a degenerative spine disease and discopathy in the lumbar segment. Similar efficacy was demonstrated in pain treatment in both discopathy and degenerative changes in the lumbosacral spine segment. This corroborated the thesis that the choice of an appropriate NSAID is the most important factor in rapid recovery.

The investigations conducted by Ekman et al. showed that the female gender is one of the important factors inducing the development of chronic pain [23]. The results of the retrospective study, as well as examinations of adult populations in Hong Kong, Norway, and Brazil [36, 37, 38] fully confirmed these data. However, no impact of patients' gender on the course of administered treatment or its effectiveness assessed after a six-week period was demonstrated. This indicates that treatment methods should be selected exclusively on the basis of the pain pathomechanism [30, 39,40, 41].

Drugs containing a dextrorotatory ketoprofen isomer exhibit a more potent analgesic and anti-inflammatory activity [42, 43]. Potentiation of the analgesic action of opioids upon administration of even sub-analgesic dexketoprofen doses has been reported from animal experiments [44]; furthermore, the drug has been found to be effective in bone metastases [45]. Additionally, it has been reported that the drug tested had a significant effect on inhibition of the wind-up phenomenon, one of the causes of chronic pain development [46]. It cannot be excluded that this mechanism may play a substantial role and be the cause of the significantly higher correlation between the changes in pain intensity and the degree of disability in patients treated with DEX.

Dexketoprofen was shown to have strong analgesic activity, both in the initial stage of the disease and later when the issue of long-term therapy efficacy, is of the greatest importance, which has been confirmed by a meta-analysis of 45 papers concerning acute and chronic pain [47].

Not only the differences between the patient groups treated with the different anti-inflammatory drugs, but also the dynamics of pain intensity changes were significant, as diclofenac in the daily dose of 100 milligrams reached the maximum effect in the third week of the treatment. This is apparently contradictory to the work of Zippel et al. [48]. who did not find differences in pain intensity in patients receiving diclofenac or dexketoprofen as a low back pain therapy. However, the presented results should not be compared, as the publication cited described treatment of acute pain, both drugs were administered via intramuscular injections, and the data analysed referred to the period immediately after drug administration. The problem requires further investigations with the use of a double-blind test.

CONCLUSIONS

Comparison of the two non-steroidal anti-inflammatory drugs demonstrated the higher efficacy of dexketoprofen in all the treatment stages; it exerted an effect on both pain intensity and the degree of disability. The significantly increased correlation between the two parameters suggests that the administration of dexketoprofen in the management of non-specific low back pain results in rapid restoration of full physical activity, and therefore a more prompt return to work.

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